REMARKS

Status of the application

Claims 1-3, 9, 11-17, 19-22, 28-36, 38-41, 47, 49-55, 57-60, 66, 68-74, 76, 85 and 95 were pending in the application. Claims 11-14, 30-33, 49-52, 68-71 were withdrawn from consideration by the Examiner as directed to non-elected inventions. Claims 1-3, 9, 15-17, 19-22, 28, 29, 34-36, 38-41, 47, 53-55, 57-60, 66, 72-74, 76, 85 and 95 were under examination in the instant Office Action . Among these examined claims, Claims 1, 2 and 15 were indicated as allowable by the Examiner, claims 3, 16, 17, 19, 21, 29, 35, 36, 38-41, 47, 53-55, 57-60, 66, 72-74, 76, 85 and 95 were rejected, and claims 9, 20, 22, 28 and 34 were objected to.

With entry of the instant response, claims 3, 21, 40, 85 and 95 have been canceled without prejudice. Claims 59 and 60 have been amended to specify that the recited dengue NS protein is the NS-1 protein. In addition, Claims 9, 20, 28, 34, 35, 38, 39, 47, 53, 54, 57-58, 66, 72, 73, and 76 have been amended to improve clarity of claim language via re-wording of existing claim language. Claims 58-60, 66, 72, 73 and 76 are also amended to specify that the claimed antibody and the reference antibody recited in the claims are monoclonal antibodies. Finally, claims 19, 38, 57 and 76 are amended to recite non-human transgenic animal. Support for these amendments is present throughout the specification, e.g., at page 17, line 27; page 20, lines 23-24; and page 23, lines 8-10. Applicants further note that, other than express disclosure, claim limitations can also be supported in the specification by implicit or inherent disclosure (See, e.g., MPEP. § 2163-I-B).

It is submitted that the claim amendments introduced herein do not contain new matter. Entry of these amendments is respectfully requested. The following remarks address in turn

the various claim objections and rejections raised in the Office Action.

Claim objections

Claims 9, 20-22, 28, 34, 35, 38, 39, 54, 55 and 72-74 were objected to by the Examiner. Specifically, claims 54, 55 and 72-74 were objected to for reciting non-elected subject matter. In response, Applicants have amended these claims to delete the recitation of nucleic acid embodiments. Claims 20-22, 28, 34 and 35 were objected to for the recitation of "all of the light chain CDR amino acids sequences of SEQ ID NO:4". These claims have been amended herein to recite the claim language as suggested by the Examiner. Similarly, Claim 38 has also been amended as suggested by the Examiner by reciting "all of the light chain CDR sequences of SEQ ID NO:4". Finally, Claim 9 has been amended herein to recite "at least one variable region comprising the amino acid sequence set forth in SEQ ID NO:4", also as suggested by the Examiner. Applicants believe these claim amendments have adequately addressed the issues raised by the Examiner.

Rejection under 35 U.S.C. §101

Claims 19, 38, 57, 76, and 95 were rejected for reciting transgenic animals. The Examiner asserts that the claims would encompass transgenic humans which are non-statutory subject matter.

The Examiner's careful review of the claims is appreciated. Claim 95 is now canceled. By inserting the "non-human" language, Applicants have amended the other noted claims as suggested by the Examiner. Withdrawal of the instant rejection is therefore urged.

Rejection under 35 U.S.C. §112

1. Claims 39, 41, 47, 53-55, 57-60, 66, 72-74 and 76 were rejected under 35 U.S.C. §112, 2nd paragraph, as allegedly being indefinite. Specifically, the Examiner states that the recitation of "at least one of SEQ ID NO:4" or "at least one light chain CDR having the amino acid sequence of SEQ ID NO:4" renders these claims indefinite.

Applicants appreciate the Examiner's careful reviewing of the claims. Though not entirely in agreement with the Examiner on this rejection, Applicants have amended the noted claims as suggested by the Examiner. Accordingly, the instant rejection should be withdrawn.

2. Claims 3, 21, 40, 59 and 60 were rejected under 35 U.S.C. §112, 1st paragraph, as allegedly not enabled. The Examiner alleges that the specification only enables antibodies that bind to dengue NS-1 but not antibodies that bind to non-NS1 dengue NS proteins.

Applicants do not agree with the Examiner's assessment of the subject disclosure in rendering the instant rejection. Nonetheless, in an effort to advance prosecution of the subject patent application, Applicants have canceled claims 3, 21 and 40. Claims 59 and 60 have also been amended herein to specify that the dengue NS protein recognized by the claimed antibodies is NS-1 protein. As such, Applicant respectfully request that the rejection be withdrawn.

3. Claims 16, 17, 29, 35, 36, 54, 55, 73 and 74 were rejected under 35 U.S.C. §112, 1st paragraph, as allegedly not enabled. The rejection is directed to the recitation in these claims of terms such as "therapeutic" or "pharmaceutical use." The

Examiner asserts that there is no evidence that the anti-NS1 antibody recited in the claims are capable of treating or prevent dengue infection, and that no effective vaccine is available. Applicants respectfully traverse this rejection.

To begin, Applicants note that the rejected claims are NOT directed to therapeutic methods of treating or preventing dengue infections. Rather, they are directed to compositions which comprise an antibody which has one or more light chain CDRs shown in SEQ ID NO:4. Although the claims have recited the term "therapeutic" or "pharmaceutic use," these terms are not elements of the claimed composition. Instead, the claims recite these terms to indicate a potential use (not the only use) the claimed compositions can have (e.g., claims 16 and 17) or the desired amount of a specific component of the composition (e.g., claim 29). It is readily apparent that patentability or enablement of the claimed compositions do not turn on these terms.

These composition claims currently rejected should be distinguished from therapeutic methods which claim use of the recited antibodies to treat or prevent dengue infections. In the latter case, the enablement issue indeed needs to address whether the recited antibodies are capable of performing the specified therapeutic functions (i.e., treating or preventing infections). In contrast, for the present composition claims, the question of enablement is whether one would be able to make and use the claimed compositions in view of the subject disclosure. The subject specification and knowledge well known in the art have surely taught how to obtain an anti-NS1 monoclonal antibody, how to prepare a composition containing such an antibody and other agents, and how to use such compositions (e.g., to diagnose infections). Therefore, the answer to the enablement question surrounding the present claims is undoubtedly in the positive.

Hence, the instant rejection should be withdrawn.

4. Claim 29 was rejected under 35 U.S.C. §112, 1st paragraph, as allegedly not complying with the written description requirement. The Examiner asserts that the claim encompasses a large genus of therapeutic or prophylactic molecules but that Applicant has not demonstrated possession of such genus of molecules. Applicants respectfully traverse the rejection.

According to the MPEP, § 2163-I-A, "[t]here is a strong presumption that an adequate written description of the claimed invention is present when the application is filed." The MPEP notes that the issue of lack of adequate written description may arise even for an original claim. However, the MPEP specifically limits such a case to situations "if the claims require an essential or critical feature which is not adequately described in the specification and which is not conventional in the art or known to one of ordinary skill in the art" (MPEP, § 2163-I-A; emphasis added). Consistently, when courts find written description problem for original claims, it is because the disclosure does not provide adequate description of certain essential or critical features of the invention being claimed. In biotechnology-related cases of the Court of Appeal for the Federal Circuit that address the written description requirement, the inventions at issue are usually directed to a genus of composition of matters (e.g., chemical compounds, polypeptides, or polynucleotides). In these cases, the composition of matters of which written description is at issue (e.g., nucleotide sequences, amino acid sequences, or compound structures) is the very subject matter being claimed, i.e., essential and critical to the claimed invention.

The Examiner is correct to note that, in order to

demonstrate possession of genus invention, the specification should disclose sufficient identifying characteristics of the claimed genus. However, the genus of therapeutic or prophylactic molecules at issue is not the claimed genus of claim 29. The instant rejection appears to have been made on an incorrect assumption that the subject invention is directed to the therapeutic or prophylactic molecules *per se*. This is certainly not the case. The rejected claim is directed to composition which comprises an isolated monoclonal antibody which has the light chain CDR sequences shown in SEQ ID NO:4. Patentability of the claimed invention resides on such specific technical features of the antibody. It does not reside on the therapeutic or prophylactic molecules recited in the claim. Rather, the recited therapeutic or prophylactic molecules are not essential or critical because the exact nature of these molecules is not important with regard to patentability of the claimed invention.

In addition, the therapeutic or prophylactic molecules are recited in the original claim when the application was filed. As such, adequate written description is provided in the specification for the recitation of these molecules in claim 29. The law of written description does not require Applicants to disclose representative members of all possible species for these non-essential features of a claimed invention. Such a requirement would surely represent a novel, unreasonable and unwarranted extrapolation of the law.

Moreover, even assuming for the sake of argument that the Examiner's position is correct, adequate description of specific species of the recited genus of therapeutic or prophylactic molecules is provided in the specification. In this regard, it must be emphasized that the specification "need not teach, and preferably omits, what is well known in the art." See

Spectra-Physics, Inc. v. Coherent, Inc., 827 F.2d 1524, 1534, 3 USPQ2d 1737, 1743 (Fed. Cir. 1987); *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1384, 231 USPQ 81, 94 (Fed. Cir. 1986). In the instant case, the various molecules recited in claim 29 are all well known in the art at the time the application was filed. One would be able to envision the structures described in each class of molecules and the activity of the molecules, e.g., analgesic, sedative, local anesthetic and etc. Further, representative species of the recited molecules are provided in the specification, e.g., in paragraphs [0107] -[0108], as well as in references which may be used to find additional molecules. Thus, there can be little doubt that one of skill in the art would conclude that there is sufficient description of the recited molecules.

For all the reasons stated above, Applicants submit that the subject specification has provided adequate written description for the presently claimed invention. Withdrawal of the instant rejection is therefore respectfully requested.

Rejections under 35 U.S.C. §102(b)

Claims 58-60 and 66 were rejected as allegedly being anticipated by Valdés et al. (Clinical and Diagnostic Laboratory Immunology, 2000, 7(5):856-857). In addition, claims 58-60, 66, 72-74, 76, 85 and 95 were rejected as allegedly being anticipated by Flamand et al. (WO 00/75665 which corresponds to US Patent 6870032). To sustain the alleged anticipation of the noted claims by the cited art, the Examiner asserts that each of these two references discloses antibodies which recognize dengue NS1 protein. In response, Applicants have canceled Claims 85 and 95 with entry of the instant response. For the reasons stated below, Applicants respectively traverse the rejections to the

extent that they are applied to the other rejected claims.

To constitute anticipation, a single prior art reference must disclose each and every element of the claimed invention. See, e.g., *Verdegaal Bros. v. Union Oil of California,* 814 F.2d 628,631,2 USPQ2d 1051,1053 (Fed. Cir. 1987); and *In re Arkley,* 172 U.S.P.Q. 524 at 526 (C.C.P.A. 1972). As detailed below, none of the cited references satisfies such legal requirements for anticipating the present claims.

First, the rejected claims have been amended herein to more clearly point out that the claimed subject matter relates to monoclonal antibodies. For example, claims 58 recites an isolated mammalian monoclonal antibody which binds to the same region as a reference monoclonal antibody having one or more of the CDRs of SEQ ID NO:4. Thus, it is abundantly clear that the rejected claims relate to monoclonal antibodies which have the same binding specificity as the reference monoclonal antibody.

As is well known in the art, specificity of a polyclonal antibody refers to the ability of the antibody to bind to a specific antigen (e.g., a protein). Thus, polyclonal antibodies directed against a given dengue NS1 protein would all be considered as having the same binding specificity. On the other hand, specificity of a monoclonal antibody refers to the ability of the antibody to specifically recognize an epitope of an antigen (e.g., a motif on a protein which usually consists of just a few amino acid residues in a three dimensional structure). It does NOT mean the ability of the antibody to merely recognize an antigen (e.g., a protein) which could potentially contain hundreds of different epitopes. Thus, two monoclonal antibodies may bind to the same protein (e.g., a NS1 protein) but do not have the same specificity because they recognize two different epitopes on the antigen. Also, when a given antigen (e.g., a NS1

protein or antigenic fragment thereof) is used as the immunogen to produce monoclonal antibodies via, e.g., hybridoma technology, a great number of antibodies with different specificities and varying affinities could potentially be generated.

The cited references merely disclose antibodies which may bind to dengue NS1 protein. There is no evidence that the antibodies would bind to the same epitope on NS1 (i.e., "the same region" as recited in the present claims) as the reference monoclonal antibodies of the subject application which have light chain CDRs shown in SEQ ID NO:4. In addition, a NS1 protein has hundreds or thousands of different epitopes against which different monoclonal antibodies recognize. Therefore, the probability that the antibodies disclosed in the cited art would happen to bind to the same epitope as the reference monoclonal antibody of the subject invention would be extremely low, if not zero. There can be no anticipation of the present claimed invention in the absence of actual evidence which indicates that the prior art antibodies bind to the same epitope as that recognized by the anti-NS1 monoclonal antibodies exemplified in the present invention.

In light of the above clarifications and claim amendment, it is readily apparent that the present claims could not be anticipated by the cited art. Withdrawal of the instant rejections is therefore respectfully requested.

CONCLUSION

In view of the foregoing, Applicants respectfully submit that the claims now pending in the subject patent application are in condition for allowance, and notification to that effect is earnestly requested. If needed, the Examiner is invited to

telephone Applicant's attorney at (858) 784-2937 to facilitate prosecution of this application.

The Director is hereby authorized to charge our Deposit Account No. 19-0962 in the event that there are any additional charges associated with the present Petition or any Response in connection with this application.

Respectfully submitted,

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Date

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